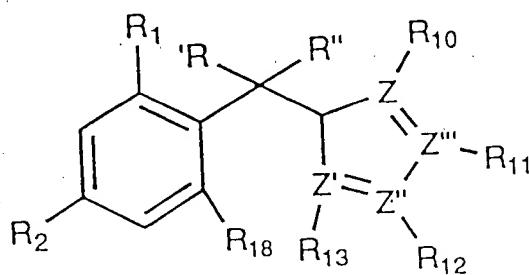
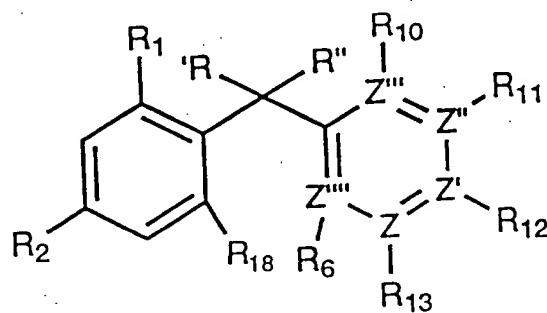


1. (Amended) A compound having the formula:



wherein

R₁ and R₂, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thioether, or amino,

or R' or R'' taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R₇R₈)N-N=, R₁₇O-N=, R₁₇N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R₆, R₁₀, R₁₁, R₁₂, R₁₃ each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈ or

$(CF)_nCF_3$, and exist only if the Z, Z', Z'', Z''', or Z'''' from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z'''' from which it originates is N,] and where one of R₆, R₁₀, R₁₁, R₁₂ or R₁₃ is X;

R₇ represents hydrogen or a lower alkyl having 1-6 carbons;

R₈ represents hydrogen or a lower alkyl having 1-6 carbons;

R₉ represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R₁₇ represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR₇ and SR₇, substituted alkenes), R₉, alkyl carboxylic acid (including halogen, acyl, OR₇ and SR₇, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR₇ and SR₇, substituted alkenes), alkyl amines (including halogen, acyl, OR₇ and SR₇, substituted alkyls), and alkenyl amines (including halogen, a[c]ryl, OR₇ and SR₇, substituted alkenes);

R₁₈ represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈, or $(CF)_nCF_3$;

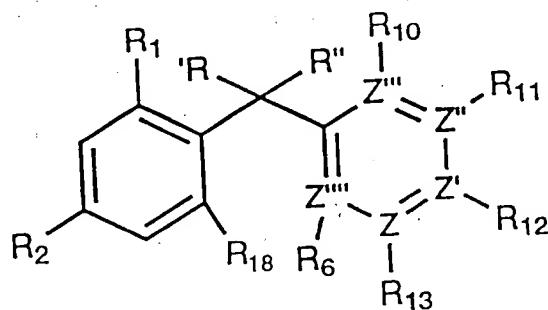
X is COOH, tetrazole, PO₃H, SO₃H, CHO, CH₂OH, CONH₂, COSH, COOR₉, COSR₉, CONHR₉, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring;

Z, Z', Z'', Z''' and Z'''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to

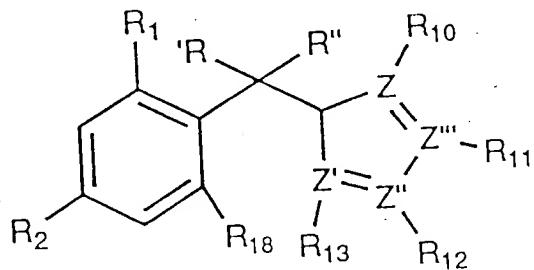
Concluded
another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N; and

n = 0-3.

4. (Twice amended) A pharmaceutical composition comprising in a pharmaceutically acceptable vehicle suitable for enteral, parenteral, or topical administration, one or more compound having the formula:



or



wherein

R₁ and R₂, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

R' and R" represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thioether, or amino,

or R' or R" taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R₇R₈)N-N=, R₁₇O-N=, R₁₇N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

*C2
C11
contd.*
R₆, R₁₀, R₁₁, R₁₂, R₁₃ each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈ or (CF)_nCF₃, and exist only if the Z, Z', Z", Z"', or Z"" from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z", Z"', or Z"" from which it originates is N,] and where one of R₆, R₁₀, R₁₁, R₁₂ or R₁₃ is X;

R₇ represents hydrogen or a lower alkyl having 1-6 carbons;

R₈ represents hydrogen or a lower alkyl having 1-6 carbons;

R₉ represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R₁₇ represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R₉, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including

halogen, acyl, OR₇ and SR, substituted alkyls), and alkenyl amines (including halogen, a [c]ryl, OR₇ and SR, substituted alkenes);

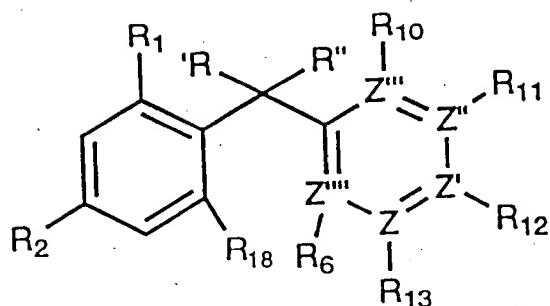
R₁₈ represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈, or (CF)_nCF₃;

X is COOH, tetrazole, PO₃H, SO₃H, CHO, CH₂OH, CONH₂, COSH, COOR₉, COSR₉, CONHR₉, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring;

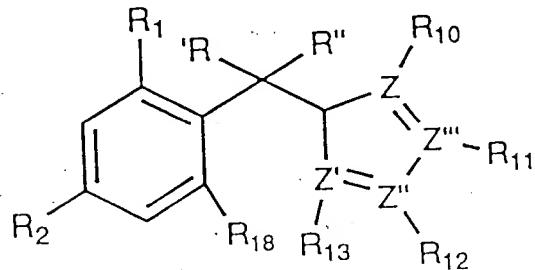
*C2
C10
contd.*
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N; and

n = 0-3

5. (Twice amended) A method for modulating a process mediated by one or more Retinoid X Receptors, said method comprising causing said process to be conducted in the presence of at least one compound having the formula:



or



wherein

R₁ and R₂, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thioether, or amino,

or R' or R'' taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R₇R₈)N-N=, R₁₇O-N=, R₁₇N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R₆, R₁₀, R₁₁, R₁₂, R₁₃ each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈ or (CF_n)_nCF₃, and exist only if the Z, Z', Z'', Z''', or Z'''' from which it originates is C, [or each independently represent hydrogen or a

lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z'''' from which it originates is N,] and where one of R₆, R₁₀, R₁₁, R₁₂ or R₁₃ is X;

R₇ represents hydrogen or a lower alkyl having 1-6 carbons;

R₈ represents hydrogen or a lower alkyl having 1-6 carbons;

R₉ represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

*C2
Contd.*

R₁₁ represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R₉, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, a[c]ryl, OR, and SR, substituted alkenes);

R₁₈ represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₈, NR₇R₈, or (CF)_nCF₃;

X is COOH, tetrazole, PO₃H, SO₃H, CHO, CH₂OH, CONH₂, COSH, COOR₉, COSR₉, CONHR₉, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring;

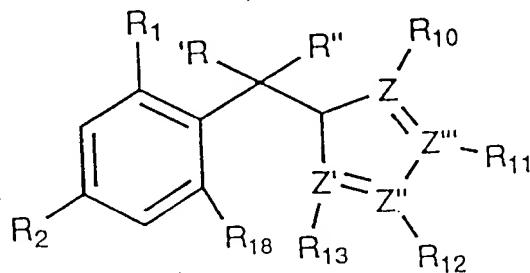
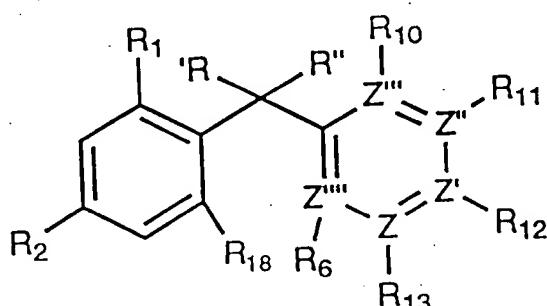
Z, Z', Z'', Z''' and Z'''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N; and

C2
Concluded

PATENT
203/270

n = 0-3.

8. (Twice amended) A method for modulating a process mediated by one or more Retinoid X Receptors, said method comprising administering to a mammalian subject an amount, effective to modulate said process mediated by said one or more Retinoid X Receptors, of one or more compound having the formula:



wherein

R₁ and R₂, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thioether, or amino,

or R' or R" taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R₇R₈)N-N=, R₁₇O-N=, R₁₇N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R₆, R₁₀, R₁₁, R₁₂, R₁₃ each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈ or (CF)_nCF₃, and exist only if the Z, Z', Z", Z'', or Z''' from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z", Z'', or Z''' from which it originates is N,] and where one of R₆, R₁₀, R₁₁, R₁₂ or R₁₃ is X;

*C³
contd*

R₇ represents hydrogen or a lower alkyl having 1-6 carbons;

R₈ represents hydrogen or a lower alkyl having 1-6 carbons;

R₉ represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R₁₇ represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R₉, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, a[c]ryl, OR, and SR, substituted alkenes);

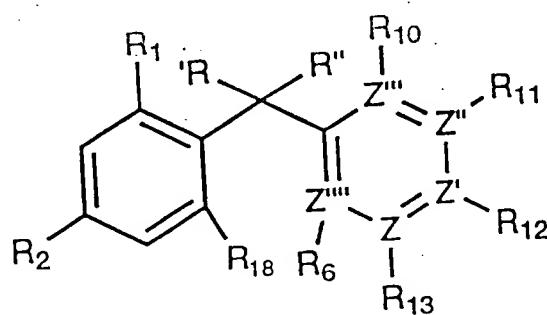
R₁₈ represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈, or (CF)_nCF₃;

X is COOH, tetrazole, PO_3H , SO_3H , CHO, CH_2OH , CONH_2 , COSH , COOR_9 , COSR_9 , CONHR_9 , or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring;

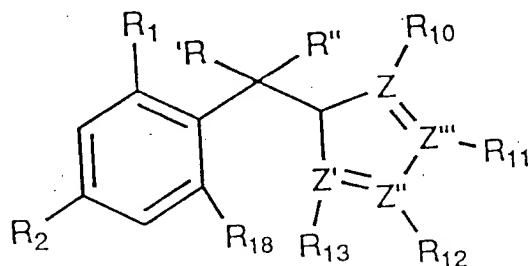
Z, Z' , Z'' , Z''' and Z'''' , each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N; and

*C³
Contd*
n = 0-3.

9. (Twice amended) A method for treating a mammalian subject requiring Retinoid X Receptor therapy comprising administering to such subject a pharmaceutically effective amount of one or more compounds having the formula:



or



wherein

R_1 and R_2 , each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thioether, or amino,

or R' or R'' taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, $(R_7R_8)N-N=$, $R_1O-N=$, $R_1N=$, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R_6 , R_{10} , R_{11} , R_{12} , R_{13} each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR_7 , SR_7 , NR_7R_8 or $(CF)_nCF_3$, and exist only if the Z , Z' , Z'' , Z''' , or Z'''' from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z , Z' , Z'' , Z''' , or Z'''' from which it originates is N,] and where one of R_6 , R_{10} , R_{11} , R_{12} or R_{13} is X;

R_7 represents hydrogen or a lower alkyl having 1-6 carbons;

R_8 represents hydrogen or a lower alkyl having 1-6 carbons;

R_9 represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q -hydroxyphenyl, q -bromophenyl, q -chlorophenyl, q -fluorophenyl, or q -iodophenyl, where $q=2-4$;

R_{17} represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR_7 and SR_7 substituted alkenes), R_9 , alkyl carboxylic acid (including halogen, acyl, OR_7 and SR_7 ,

substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR, and SR, substituted alkyls), and alkenyl amines (including halogen, a [c]ryl, OR, and SR, substituted alkenes);

C³
CON
ff

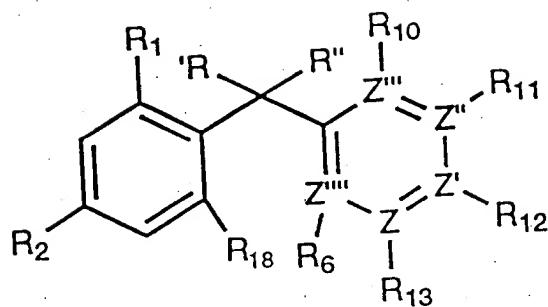
R₁₈ represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈, or (CF)_nCF₃;

X is COOH, tetrazole, PO₃H, SO₃H, CHO, CH₂OH, CONH₂, COSH, COOR₉, COSR₉, CONHR₉, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring;

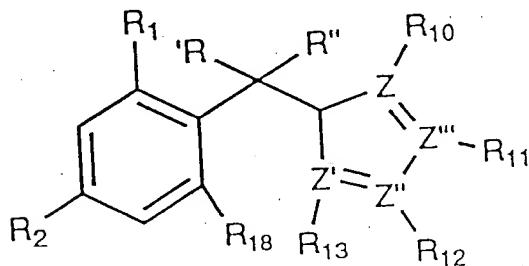
Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N; and

n = 0-3.

10. (Twice amended) A method for increasing plasma concentrations of high density lipoprotein in a mammalian subject comprising administering to such subject a pharmaceutically effective amount of one or more compounds having the formula:



or



wherein

R₁ and R₂, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

R' and R'' represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thioether, or amino,

or R' or R'' taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R₇R₈)N-N=, R₁₇O-N=, R₁₇N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

R₆, R₁₀, R₁₁, R₁₂, R₁₃ each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈ or (CF)_nCF₃, and exist only if the Z, Z', Z'', Z''', or Z'''', from which it originates is C; or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z'', Z''', or Z''''' from

which it originates is N,] and where one of R₆, R₁₀, R₁₁, R₁₂ or R₁₃ is X;

R₇ represents hydrogen or a lower alkyl having 1-6 carbons;

R₈ represents hydrogen or a lower alkyl having 1-6 carbons;

R₉ represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

*13
Contd.*
R₁₇ represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R₉, alkyl carboxylic acid (including halogen, acyl, OR₇, and SR₇, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including halogen, acyl, OR₇, and SR₇, substituted alkyls), and alkenyl amines (including halogen, a[c]ryl, OR, and SR, substituted alkenes);

R₁₈ represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈, or (CF)_nCF₃;

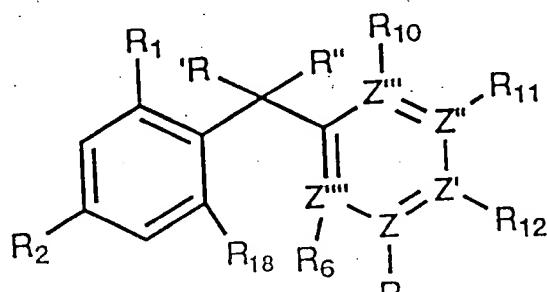
X is COOH, tetrazole, PO₃H, SO₃H, CHO, CH₂OH, CONH₂, COSH, COOR₉, COSR₉, CONHR₉, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring;

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N; and

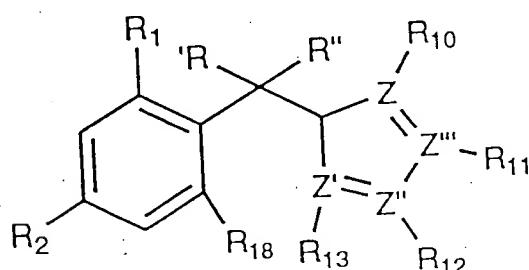
n = 0-3.

11. (Twice amended) A method for modulating a process mediated by intracellular receptors, said method comprising causing said process to be conducted in the presence of a composition comprising a first compound as set forth below which selectively activates Retinoid X Receptors in preference to Retinoid Acid Receptors, in combination with a second compound which activates one or more intracellular receptors other than Retinoid X Receptors, and wherein the physiological effect in mammals produced by said composition at a given concentration is greater than the additive effect achieved by utilizing each said compound alone at said concentration, said first compound having the formula:

*C3
Cont'd
115/2*



or



115/2
wherein

R₁ and R₂, each independently, represent hydrogen or lower alkyl or acyl having 1-4 carbon atoms;

R' and R" represent hydrogen, lower alkyl or acyl having 1-4 carbon atoms, OH, alkoxy having 1-4 carbon atoms, thiol or thioether, or amino,

or R' or R" taken together form an oxo (keto), methano, thioketo, HO-N=, NC-N=, (R₇R₈)N-N=, R₁₇O-N=, R₁₇N=, epoxy, cyclopropyl, or cycloalkyl group and wherein the epoxy, cyclopropyl, and cycloalkyl groups can be substituted with lower alkyl having 1-4 carbons or halogen;

*C 3
Contd.*
R₆, R₁₀, R₁₁, R₁₂, R₁₃ each independently represent hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈ or (CF)_nCF₃, and exist only if the Z, Z', Z", Z"', or Z"" from which it originates is C, [or each independently represent hydrogen or a lower alkyl having 1-4 carbons if the Z, Z', Z", Z"', or Z"" from which it originates is N,] and where one of R₆, R₁₀, R₁₁, R₁₂ or R₁₃ is X;

R₇ represents hydrogen or a lower alkyl having 1-6 carbons;

R₈ represents hydrogen or a lower alkyl having 1-6 carbons;

R₉ represents a lower alkyl having 1-4 carbons, phenyl, aromatic alkyl, or q-hydroxyphenyl, q-bromophenyl, q-chlorophenyl, q-fluorophenyl, or q-iodophenyl, where q=2-4;

R₁₇ represents hydrogen, lower alkyl having 1-8 carbons, alkenyl (including halogen, acyl, OR, and SR, substituted alkenes), R₉, alkyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkyls), alkenyl carboxylic acid (including halogen, acyl, OR, and SR, substituted alkenes), alkyl amines (including

halogen, acyl, OR₇ and SR₇ substituted alkyls), and alkenyl amines (including halogen, a[c]ryl, OR₇ and SR₇ substituted alkenes);

R₁₈ represents hydrogen, a lower alkyl having 1-4 carbons, halogen, nitro, OR₇, SR₇, NR₇R₈, or (CF)_nCF₃;

*C 3
Concluded*
X is COOH, tetrazole, PO₃H, SO₃H, CHO, CH₂OH, CONH₂, COSH, COOR₉, COSR₉, CONHR₉, or COOW where W is a pharmaceutically acceptable salt, and where X can originate from any C or N on the ring;

Z, Z', Z'', Z''' and Z''', each independently, represent C, S, O, N, or a pharmaceutically acceptable salt, but is not O or S if attached by a double bond to another such Z or if attached to another such Z which is O or S, and is not N if attached by a single bond to another such Z which is N; and

n = 0-3.

REMARKS AND PETITION

Applicants request amendment, as shown above, in claim 1 and likewise in claims 4-5 and 8-11, of the definition of R₆, R₁₀, R₁₁, R₁₂, R₁₃ to delete the phrase in the 4th thru 6th lines of the definition, which deletion eliminates non-existent compounds. In addition, applicants request correction of the spelling of q-fluorophenyl in the third line of the definition of R₉, and also request correction of the spelling of aryl in the last line of the definition of R₁₇, in each of claims 1, 4-5 and 8-11.

Amendment is requested pursuant to 37 CFR § 1.312(b), and applicants hereby petition that this amendment be entered. The